Neoplasia

By

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Neoplasia

1-Basic concepts

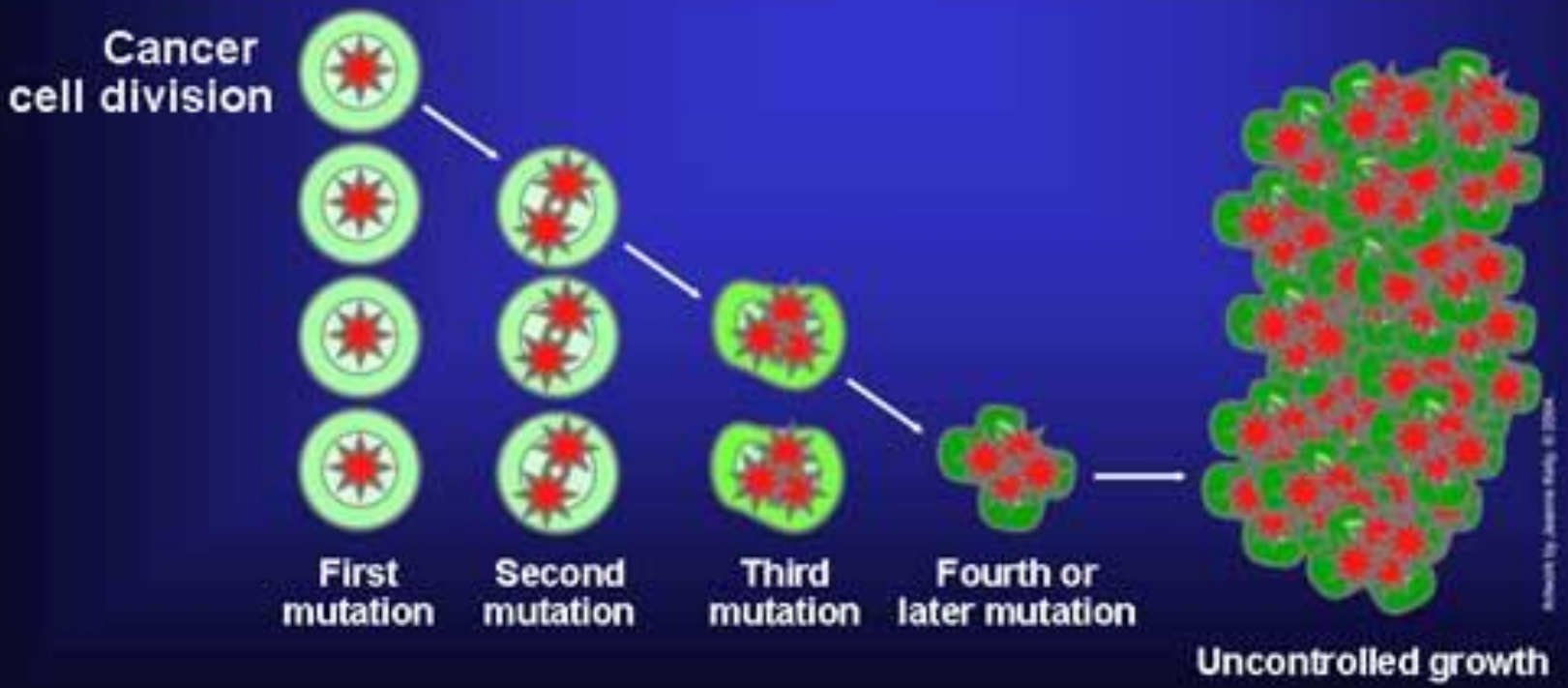
Neoplasia

Abnormal mass of tissue:

- the growth of which exceeds and is uncoordinated with normal tissue.
- Uncontrolled by the normal growth control.
- Competes with normal cells for metabolic needs

= Autonomous new growth

Loss of Normal Growth Control



General features:

- Named by suffix oma
- Originate from any cell
- Result from mutation
- Composed of cells and stroma
- Classified according to cell of origin and behaviour

Structure

Each tumor - Benign or malignant- has two basic components

-**Parenchyma**…proliferating neoplastic cells.

-**Supportive stroma**; connective tissue and blood vessels.

Structure

1- Parenchyma

* Made of transformed or neoplastic cells

* It determines the biological behavior of the tumor (benign or malignant)
*From it the tumor derives its name.
*The tumor results from **clonal proliferation of a single cell (Monoclonal).** Therefore, the more the cell divides, the more its chance for tumor production.

Structure

2-Supporting stroma

* It is host derived, non-neoplastic component of the tumor.

*It is made of connective tissue and blood vessels of the tumor.

*Vascularity is related to tumor-angiogenesis factors (TAFs) which are mainly produced by the tumor cells.

Classification of tumors

According to the biological behavior

A) Benign

B) Malignant

C) Locally malignant

According to the tissue of origin

A) Epithelial(Adenoma, papilloma - Carcinoma)

B) Mesenchymal (….oma - Sarcoma

C) Miscellaneous

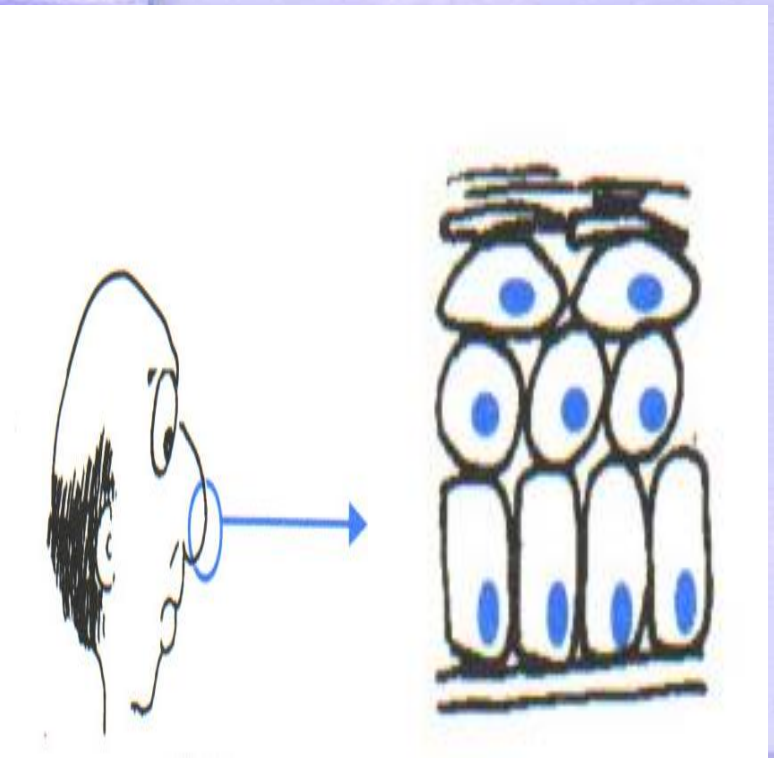
Nomenclature of neoplasms

1- Surface epithelium

Squamous

Benign

Malignant



Sq. Papilloma

Sq.Carcinoma

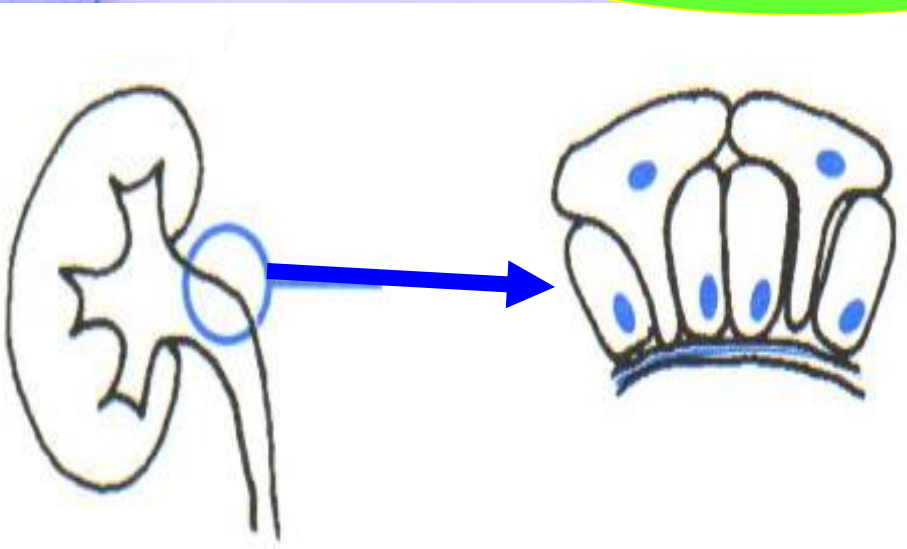
Transitional

Benign

Malignant

Tran. Papilloma

Trans Carcinoma



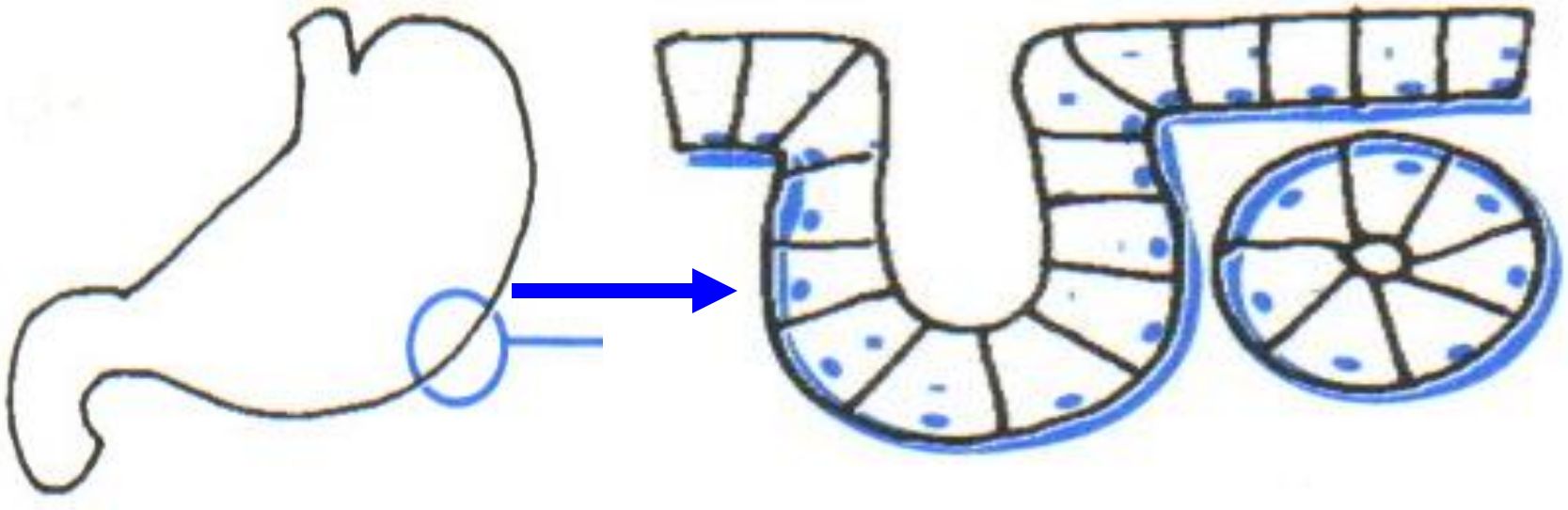
2- Glandular epithelium

Benign

Adenoma

Malignant

Adenocarcinoma

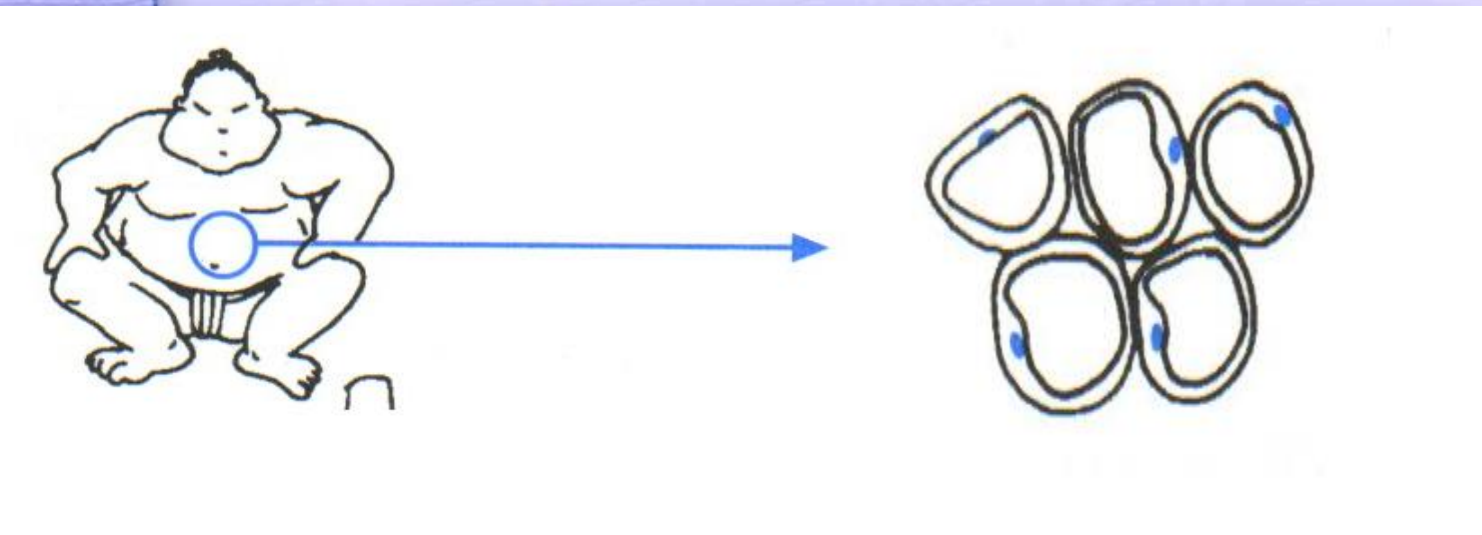


Mesenchymal tissue

Fat

Benign → Lipoma

Malignant → Liposarcoma

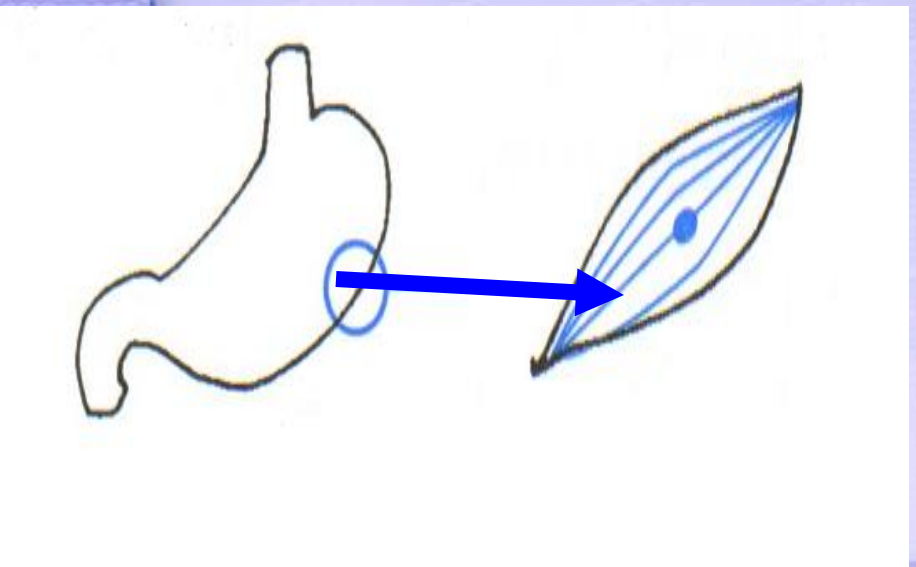


Mesenchymal tissue

Smooth Muscle

Benign → Leimyoma

Malignant → Leiomyosarcoma

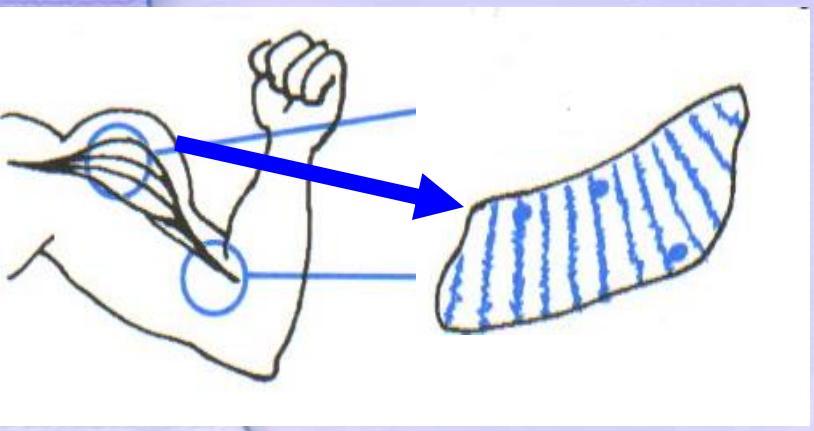


Mesenchymal tissue

Skeletal Muscle

Benign

Malignant



Rhabdomyosarcoma

Rhabdomyoma

Mesenchymal tissue

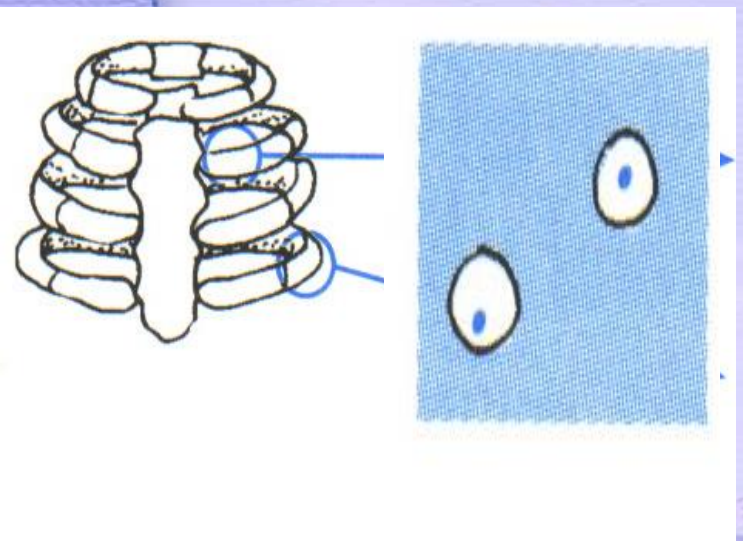
Cartilage tissue

Benign

Malignant

Chondroma

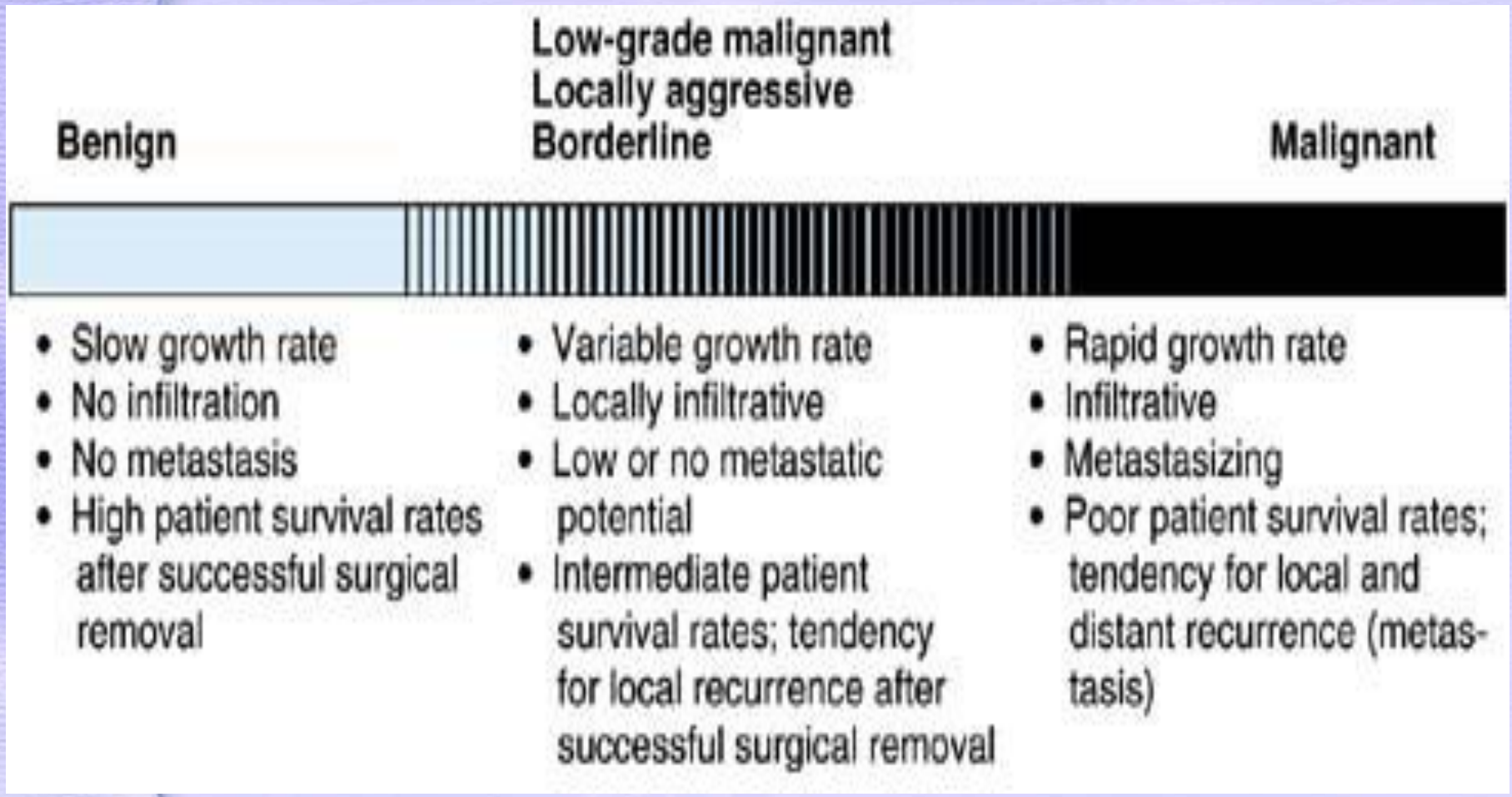
Chondrosarcosarcoma



Differences between benign and malignant tumors

- ☆ Rate of growth
- ☆ Mode of growth.
- ☆ Gross appearance No., size , capsule, consistency, C/S .. vascularity and secondary changes.
- ☆ Microscopic appearance.. Cytology, histology, stroma, secondary changes.
- ☆ Spread
- ☆ Prognosis

Benign Vs Malignant tumors

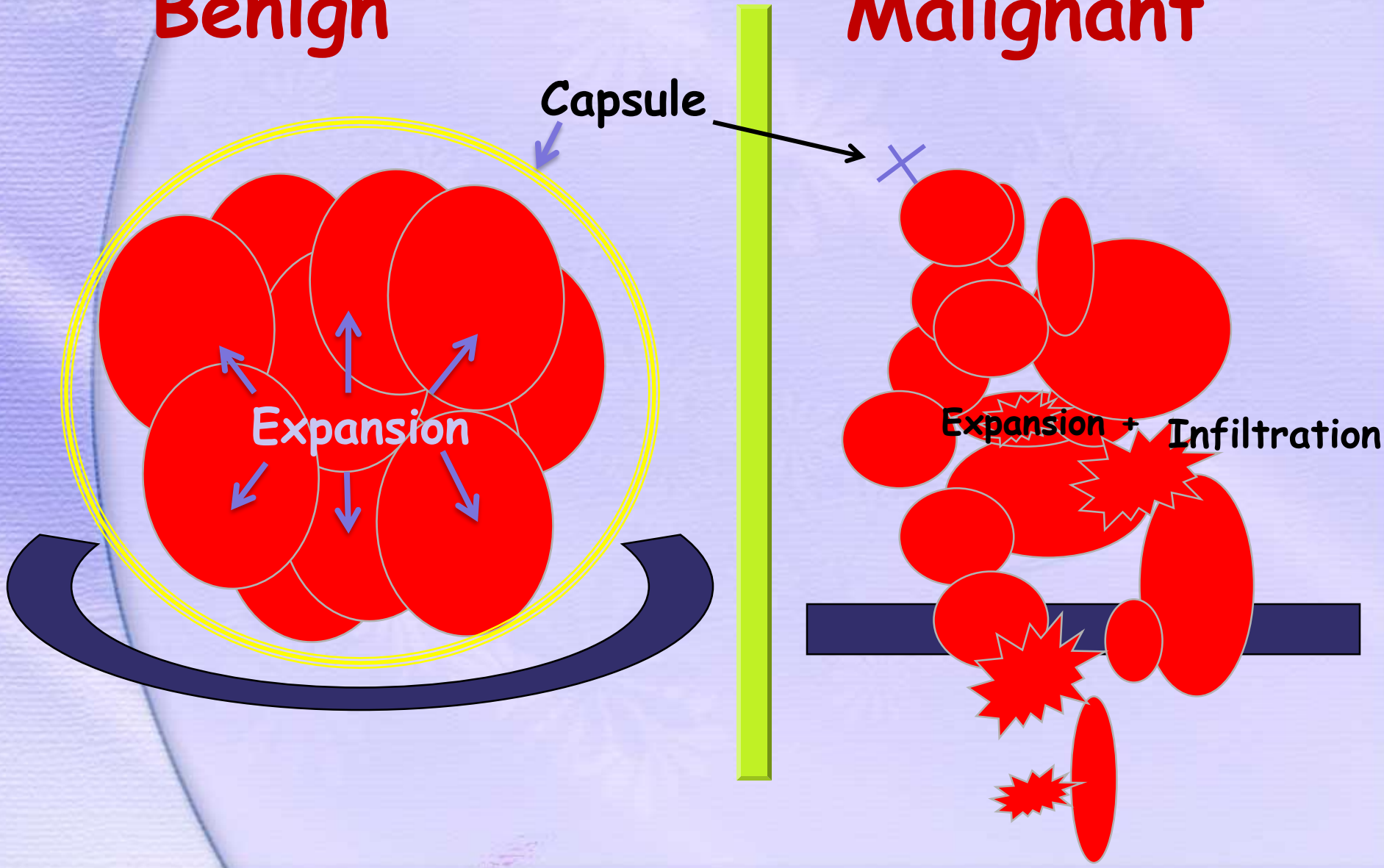


BENIGN TUMOR	MALIGNANT TUMOR
1. Definition	
A single mass formed of mature tissue, slowly growing and remains localized.	A mass formed of imperfectly mature tissue, grows rapidly, and invades the surrounding structures, lymphatic and blood vessels to form 2ry (metastatic) tumors.
2. Origin	
Normal cells(de novo).	De novo or from premalignant lesion.
3. Rate of growth	
Slow.	Rapid.
4. Mode of growth	
Expansion i.e. pushing the surrounding normal tissue without invasion.	Expansion and infiltration i.e. destroy and invade the surrounding normal tissue.

Mode of growth

Benign

Malignant



BENIGN TUMOR	MALIGNANT TUMOR
5. Gross features	
a. Number: single.	**a. Number:** begin single and metastasize.
b. Size: usually small.	**b. Size:** reach a large size within a short time.
c. Capsule: capsulated. (Surface epithelial benign tumors, leiomyoma and osteoma are exceptions).	**c. Capsule:** absent, noncapsulated.
d. Cut section: uniform, no hemorrhage or necrosis.	**d. Cut section:** usually solid vascular, shows secondary changes as hemorrhage and necrosis.

BENIGN TUMOR	MALIGNANT TUMOR
5. Gross features	
e. Shape: according to the site; • Inside solid organ or connective tissue, it is globular or ovoid surrounded by fibrous capsule. • Arise from surface epithelia it forms a **noncapsulated polyp (papilloma).**	**e. Shape:** according to the site; • Inside solid organ, as irregular noncapsulated mass. • In connective tissue; it is coarsely nodular mass • Arise from surface epithelia, takes different forms; **1. Polypoid fungating mass** **2. Ulcerative pattern (malignant ulcer)** **3. Infiltrative growth pattern (*annular*)**

Benign Neoplasms

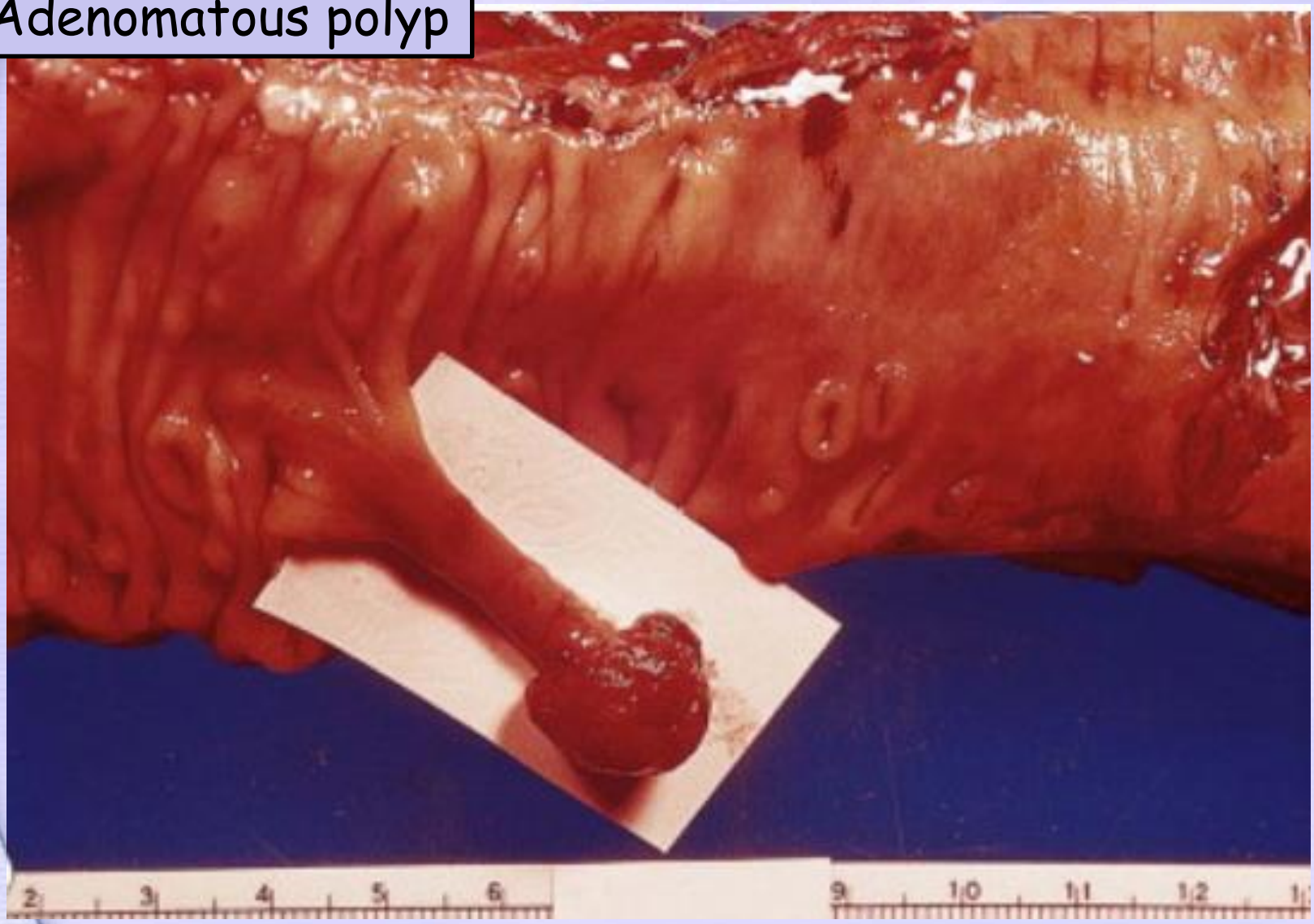
Thyroid adenoma

Benign Neoplasms

Lipoma

Benign Neoplasms

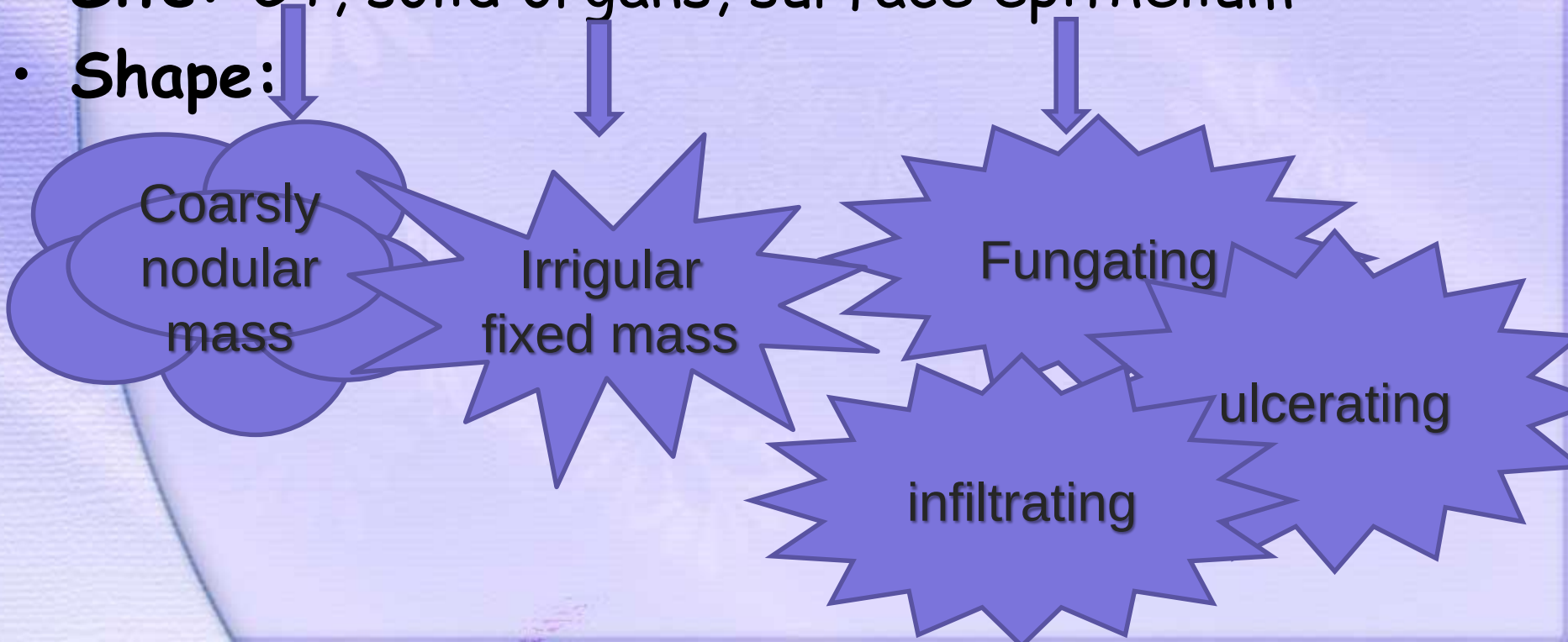
Adenomatous polyp



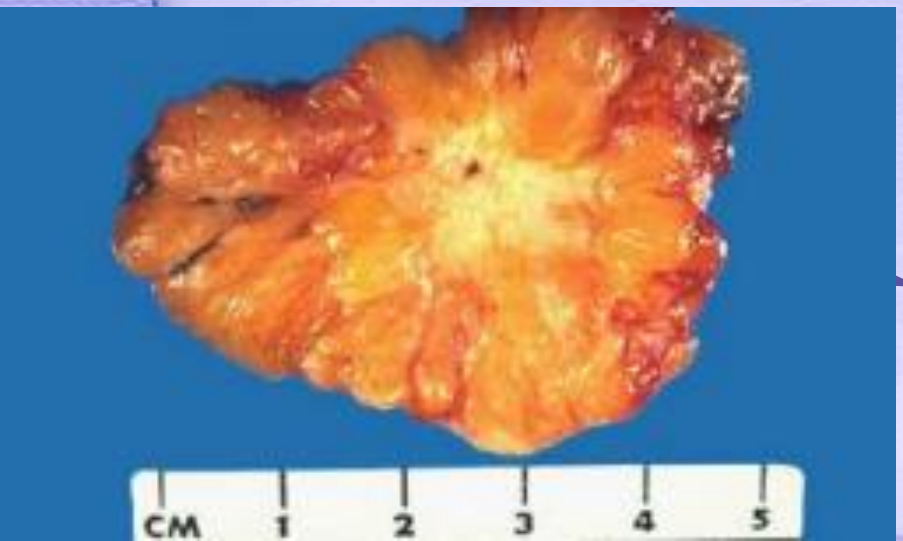
Malignant Neoplasms

Gross:

- **Number:** start single
- **Size:** Large over short duration
- **Site:** CT, solid organs, surface epithelium
- **Shape:**



Malignant Neoplasms

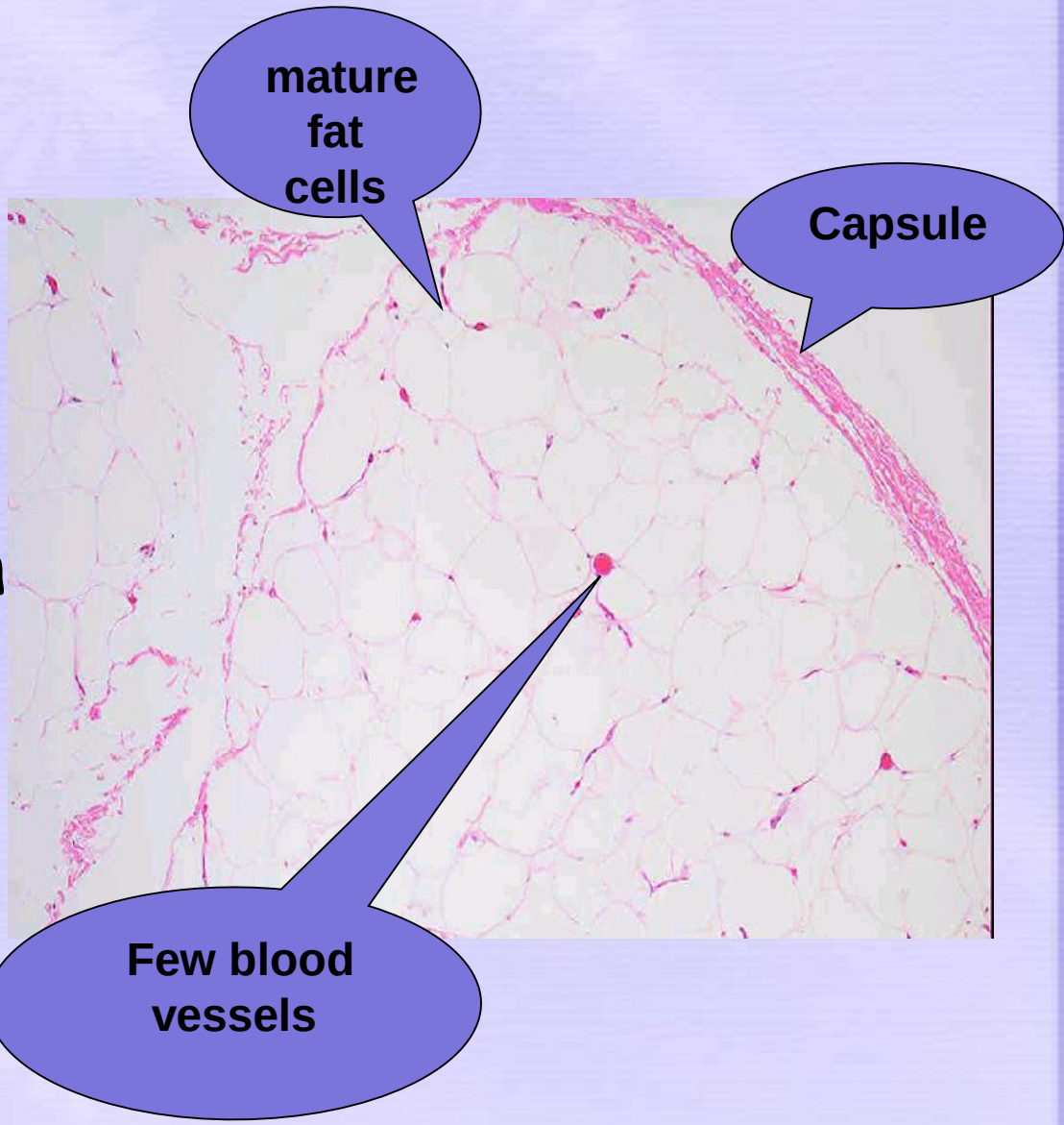


BENIGN TUMOR	MALIGNANT TUMOR
6. Microscopic features	
1. Cytology: the cells are: • Mature, resemble the mother cells. • With minimal mitoses.	**1.Cytology:** the cells show cytologic criteria of malignancy (***cellular anaplasia)***
2. Histology (the pattern of arrangement): The pattern assumed by the tumor cells is similar to the tissue of origin e.g. thyroid adenoma is formed of thyroid acini similar to the normal thyroid acini.	**2. Histology (the pattern of arrangement):** *depends on the tumor grade.* ***Tumor Grade:*** the degree of resemblance of the tumor to the mother tissue as regard morphology and function.
3. Stroma: • Well formed with few blood vessels. • 2ry changes may occur. • No hemorrhage or necrosis.	**3. Stroma:** • Poor, with prominent vascularity. • The secondary changes are common. • Hemorrhage and necrosis are common.

Benign Neoplasms

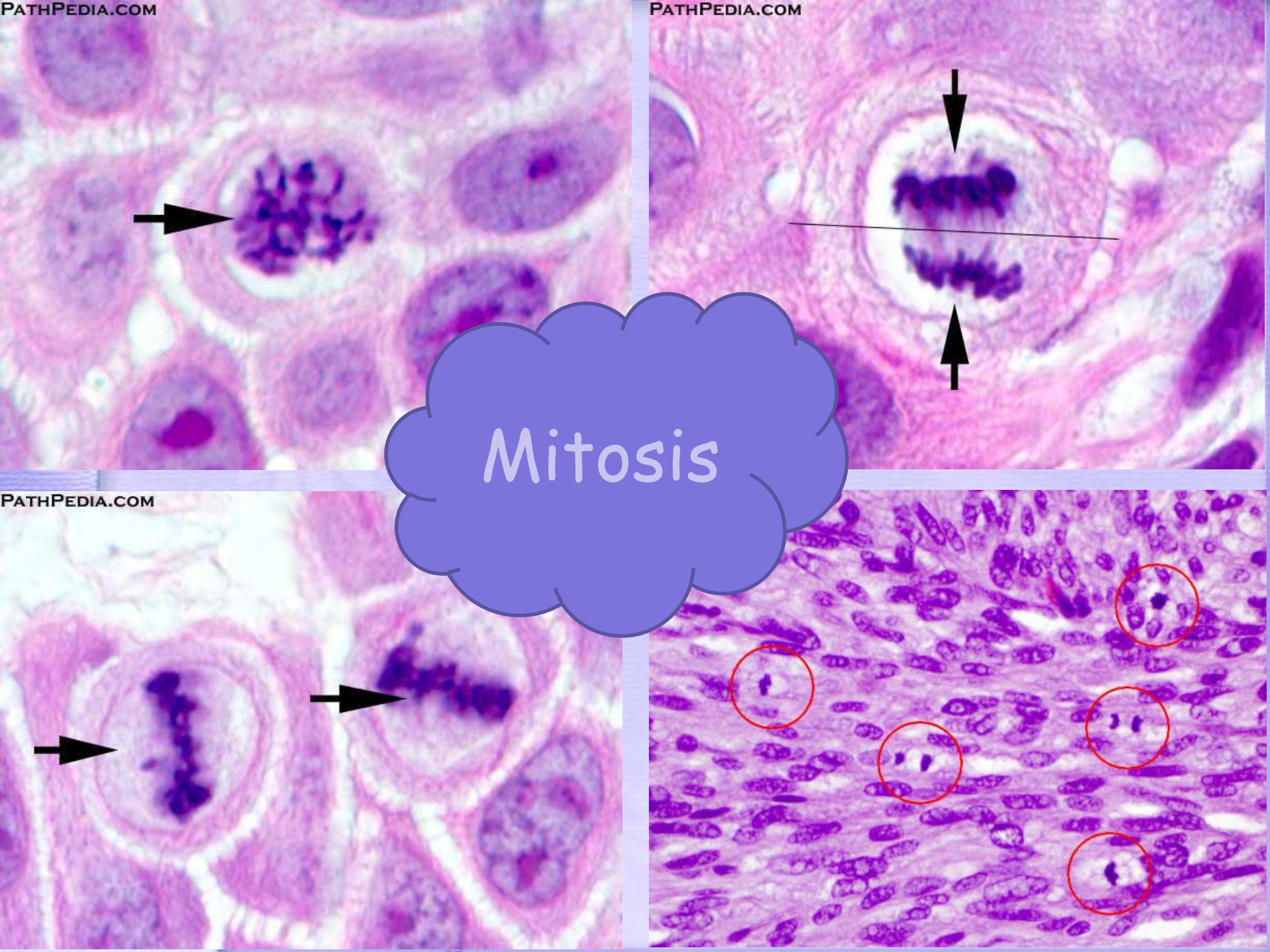
Lipoma

- In benign tumors Individual cells are mature.
  - They resemble more or less the mother cell of origin
  - Minimal mitoses.
  - Few well formed blood vessels.
- Minimal secondary changes

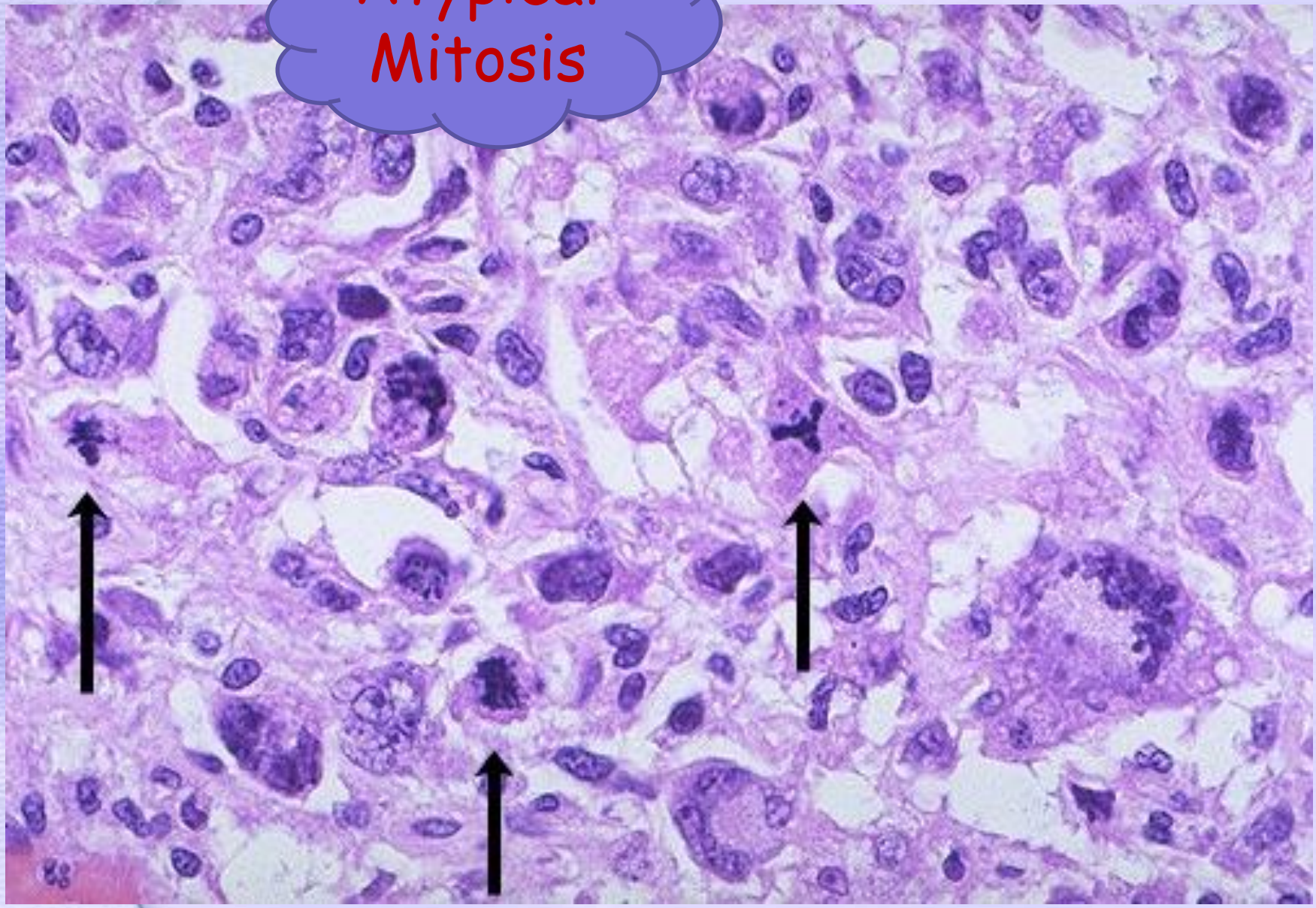


Malignant cells show….. ANAPLASIA

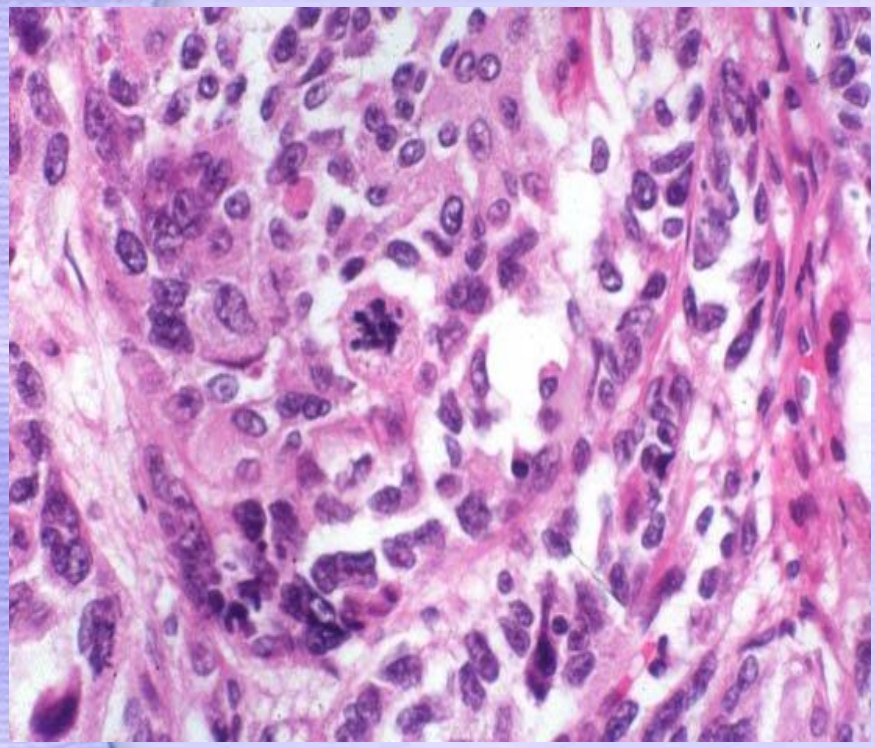
- **Pleomorphism** = variability in size& shape of cells and nuclei.
- **Hyperchromatism** = increased D.N.A. inside the nucleus for cell division----- stain more with heamatoxylin.
- **Increased N/C ratio** to1/2 (N = 1/4)
- **Prominent nucleoli**
- **Increased mitotic figures** with abnormal mitoses. Nuclear division without the cytoplasm- leads to tumor giant cells.
- **Loss of polarity**
- **Tumor giant cells**

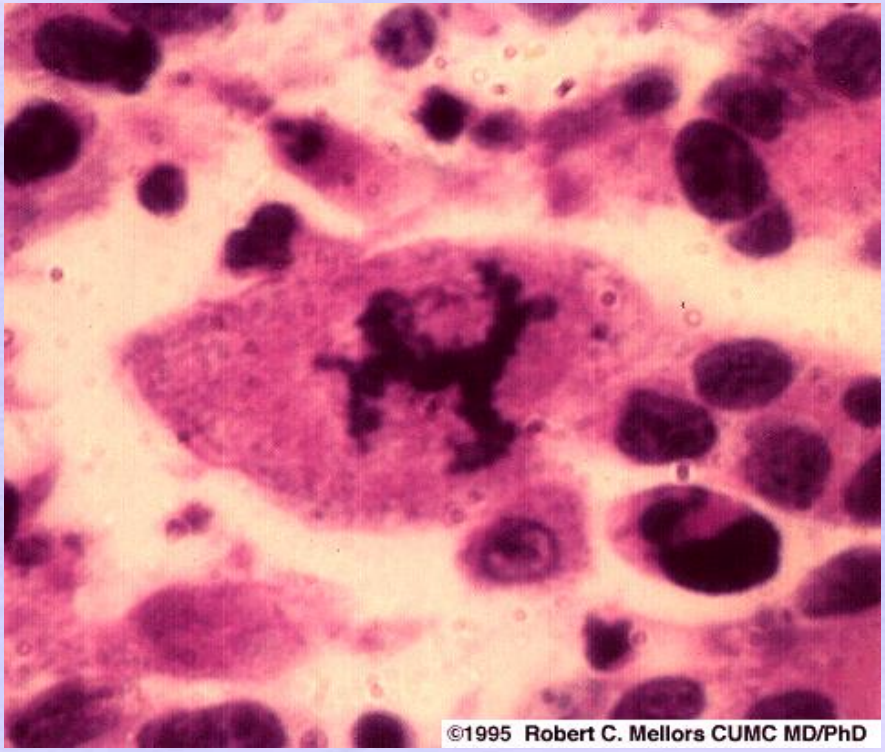

PathPedia.com
PathPedia.com
Mitosis
PathPedia.com

Atypical Mitosis

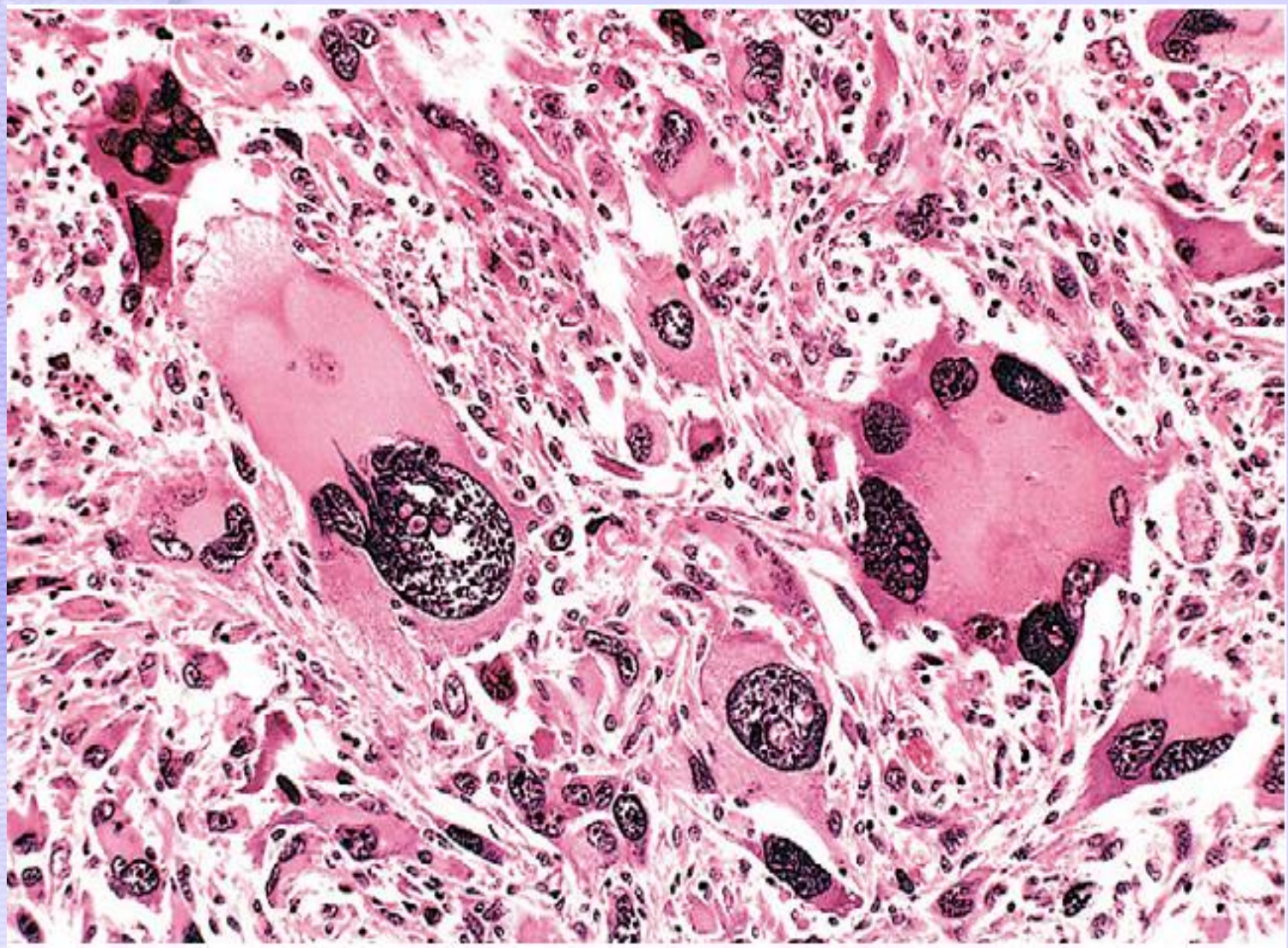


Malignant Neoplasms





Cytological criteria of malignancy
=Anaplasia



Rate of Growth

-Benign tumors grow slowly over a period of years

-Malignant tumors grow rapidly and erratically

- Most malignant tumors grow more rapidly than benign tumors.

- Growth rate correlates with level of differentiation.

Differentiation

-The extent to which parenchymal cells of the tumor resemble comparable normal cells, both morphologically and functionally (degree of resemblance to the tissue of origin).

-Well differentiated tumors, composed of cells resembling mature tissue

-Poorly differentiated , undifferentiated tumors have primitive appearing, unspecialized cells.

- **Benign tumors** are well differentiated
- **Malignant tumors** range from well differentiated to undifferentiated

If cells LOOK GOOD, they are probably going to BEHAVE GOOD

Looking "good" means looking like the cells they supposedly arose from!

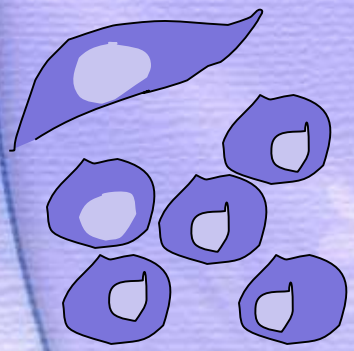
If cells LOOK BAD, they are probably going to BEHAVE BAD

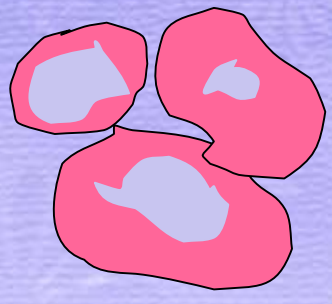
Looking "bad" means NOT looking like the cells they supposedly arose from!

Tumor Grade

- Based on microscopic features (cytology or histology)

- It is the degree of resemblance of tumor cells to their mother cell origin both morphologically and functionally.





Low grade	Intermediate grade	High grade

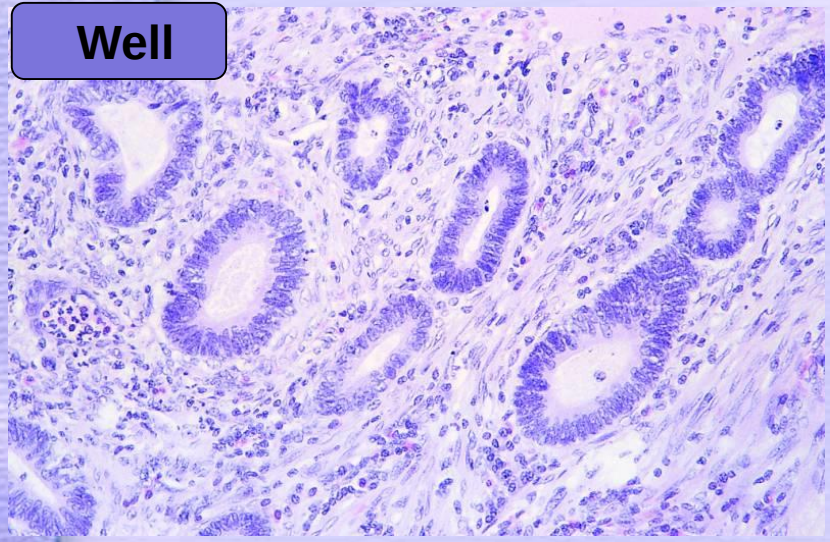
Grading of Tumors

- Tumor **GRADE =**
  degree of resemblance of the tumor to mother tissue as regards morphology , function, and relationship to themselves and other cells.
  - It may be:- *Well differentiated
    *Moderately diff. *Poorly diff .
  *Undifferentiated or anaplastic.

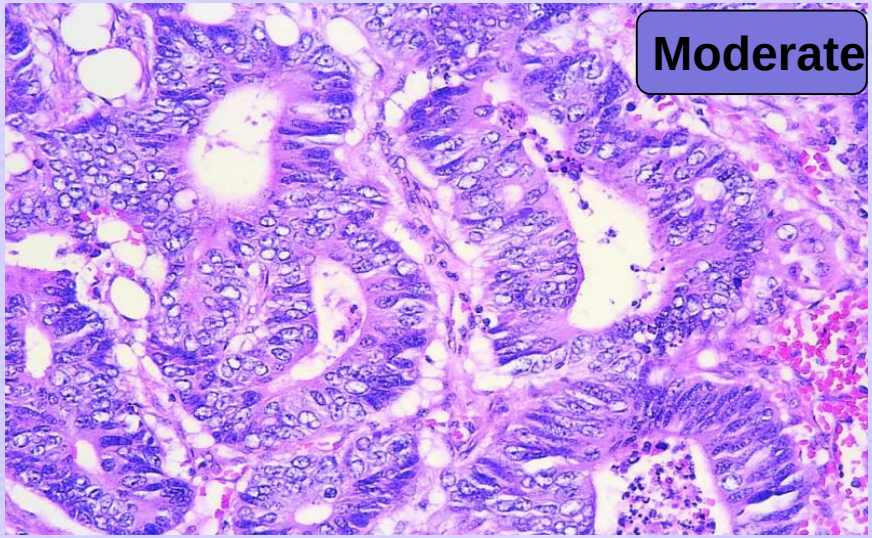
- **The degree of malignancy increases with decreased differentiation .**

Tumor grade

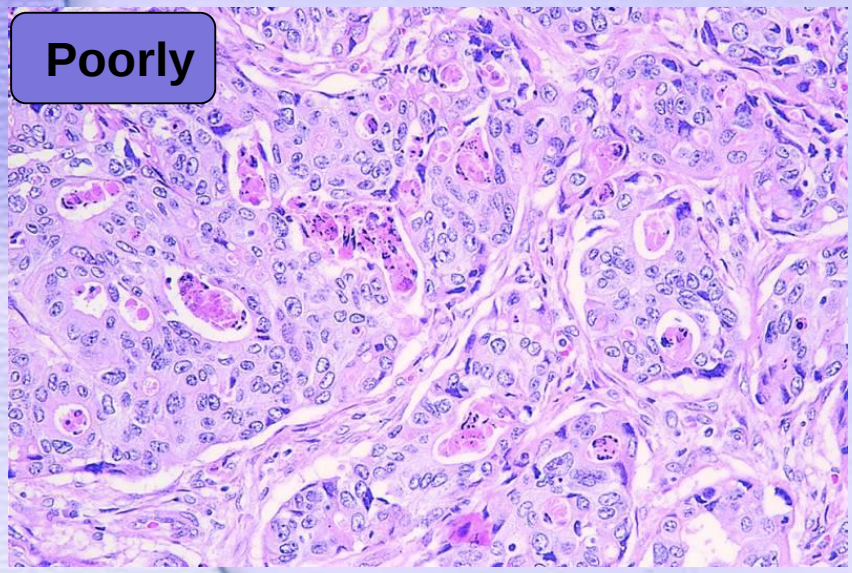
Well



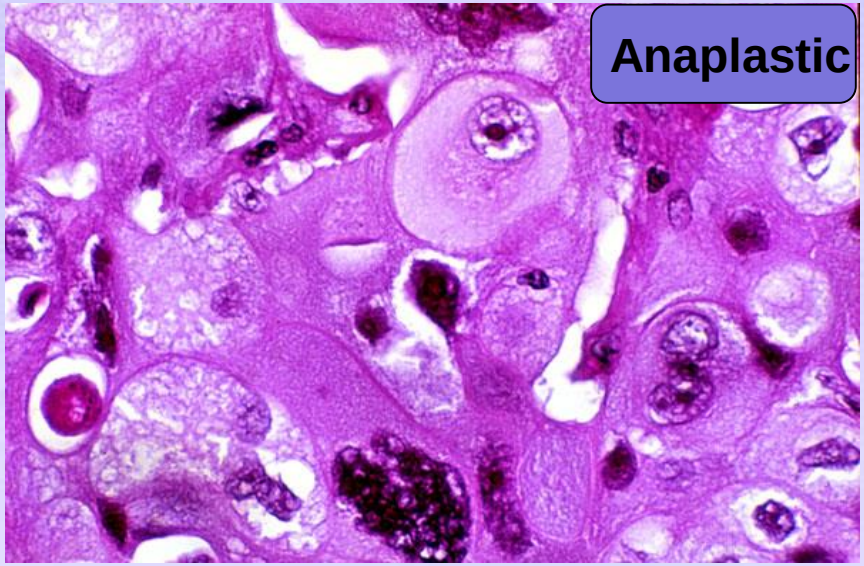
Moderate



Poorly



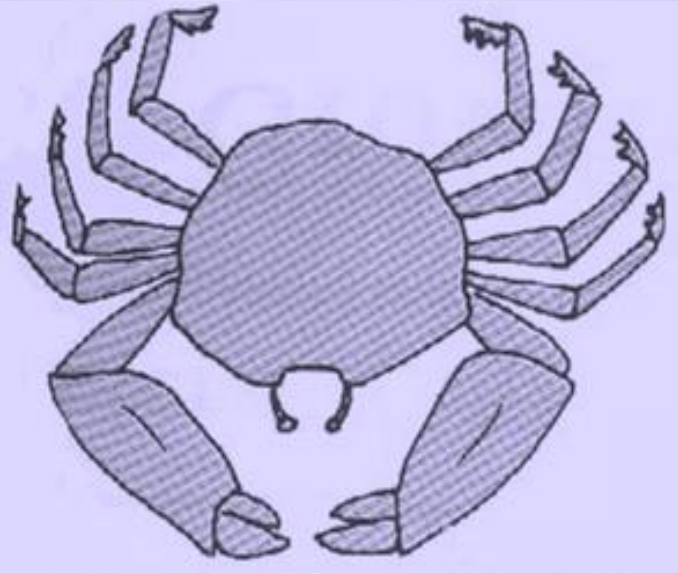
Anaplastic




Thank You

BENIGN TUMOR	MALIGNANT TUMOR
7. Behavior & Prognosis	
1. Don't spread. 2. Don't recur if well excised. 3. Don't endanger patient life except in the following conditions: a. Located in vital organ. b. Located in tubular organ (obstruction). c. Produce hormones. d. Change malignant.	1. Spread. 2.Recur. 3.Endanger patient life due to: a. Local organ destruction due to direct spread. b. Destruction of distant organs by distant spread. c. Obstruction of hollow organs. d. Paraneoplastic syndrome. e. Anaemia. f. Cachexia.

Malignant Neoplasms



Behaviour:

- Rate of growth
- Mode of growth.
- ***Spread***

  *Local

  Distant metastasis **Surest sign of malignancy**
- ***Recurrence***
- ***Prognosis:*** Fatal

  *Cachexia *Immune supression

  * Destruction of distant organs (metastasis)

Locally Malignant Neoplasms

Tumors which infiltrate locally but don't the capacity to send distant metastases.

- ***Growth:*** Slow
- ***Mode of growth:*** infiltrative
- ***N/E:*** noncapsulated
- ***M/E:*** cells are malignant
- ***Spread:*** local only, No metastasis
- ***Prognosis:***

  *Recur after incomplete excision

  *May turn malignant (metastasizing)

Basal cell carcinoma

Rodent ulcer

sites
Gross
margin
Edge
Floor
Base

Malignant epithelial tumors
CARCINOMA

Definition: Malignant tumor of the surface epithelium. Ex: Squamous cell carcinoma, adenocarcinoma

Incidence: More common than sarcoma

- **Age:** Middle and old
- **Rate of growth:** Slower than sarcoma
- **Mode of growth:** Infiltrate than expand
- **Spread:** early by lymphatics late, by blood.

Malignant mesenchymal tumors SARCOMA

Definition: Malignant tumor of the surface epithelium. Ex: Squamous cell carcinoma, adenocarcinoma

- **Incidence:** Less common than carcinoma
  Occur in young age
- **Rate of growth:** higher than carcinoma
- **Mode of growth**: by expansion than by infiltration.
- **Spread:** Spreads early by blood.

Spread of tumors

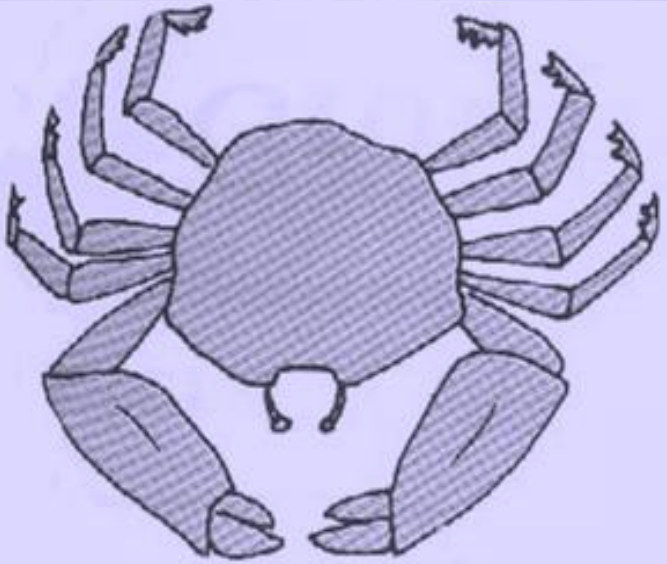
Benign tumors do not spread.

Malignant tumors spread by:

- Local
- Metastasis

Invasion and Metastasis

- Characteristics that are unique to malignant neoplasms (cancer)
- the most reliable feature that differentiates malignant from benign tumors.
- The major cause of morbidity and mortality



Spread of malignant tumors

*Local" invasion"

- It is the presence of tumor cells away from their site of origin without loss of continuity with the primary.

Invasion of the extracellular matrix; E.C.M in basement membrane & interstitium.

*Distant "metastasis"

- It is the presence of tumor cells away from the primary without continuity with it.

- Lymphatic
- Blood
- Transcoelomic (through serous sacs)
-Through natural passages
-Implantation

Metastasis

-Tumor implants discontinuous with the primary tumor

-Unequivocally marks a tumor as malignant because benign tumors do not metastasize, also, locally malignant tumors have no capability for metastasis

-All cancers can metastasize but with variable tendencies.

-30% of newly diagnosed patients with malignant tumors, present with metastases

Hematogenous Spread

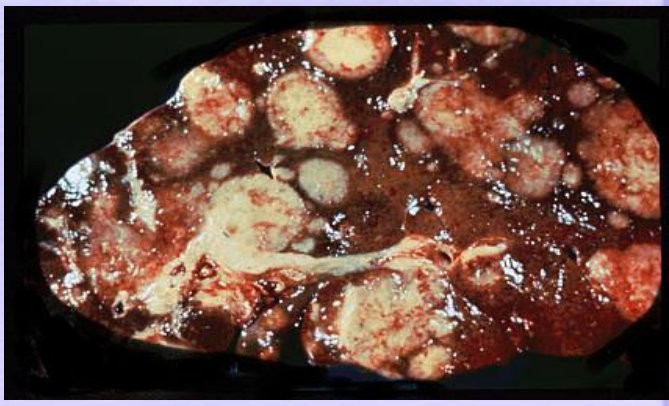
- Typical of sarcomas, can be used by carcinomas

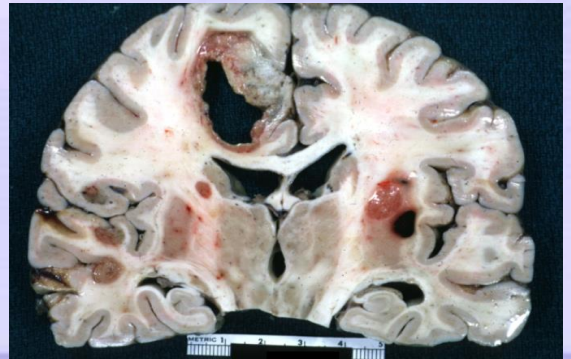
Angiogenesis→
Adhesion to BM→
BM Invasion→
Intravasation→
Embolization→
Adhesion to BM→
Extravasation→
METASTATIC GROWTH

Homing of tumor cells

Favorable sites

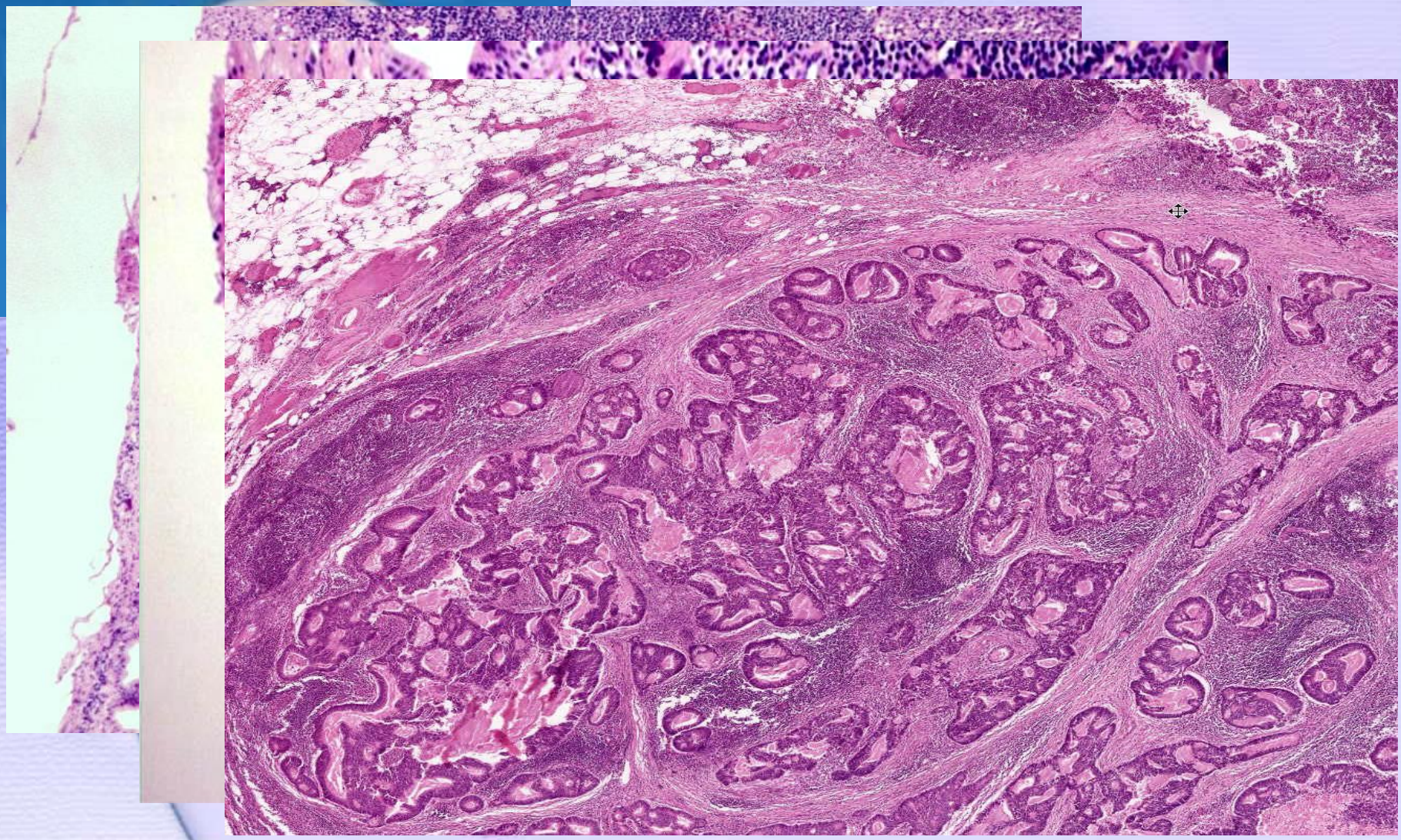
- LUNGS
- LIVER
- BONE MARROW
- BRAIN
- ADRENAL GLANDS





Lymphatic Spread

Lymphatic embolism



Trans coelomic

Occurs whenever a malignant neoplasm penetrates into an "open field"
-peritoneal cavity
-pleural cavity
-pericardial cavity
-subarachnoid space

Systemic Effects of Cancer in the Host

- Most symptoms of cancer are due to local effects of primary tumor or its metastases ⇨ **Neoplastic syndrome.**

- In some patients, cancer produces remote effects not caused by invasion or metastases ⇨ **paraneoplastic syndromes.**

Cachexia

- characteristic wasting syndrome seen in CA patients. Anorexia, weight loss, lethargy

- Causes…

a. Inadequate food intake

b. Impaired digestion, absorption

c. Competition between host and tumor for nutrient? - unlikely

d. Increased energy requirement of CA patient -elevated metabolic rate

e. TNF, other cytokines

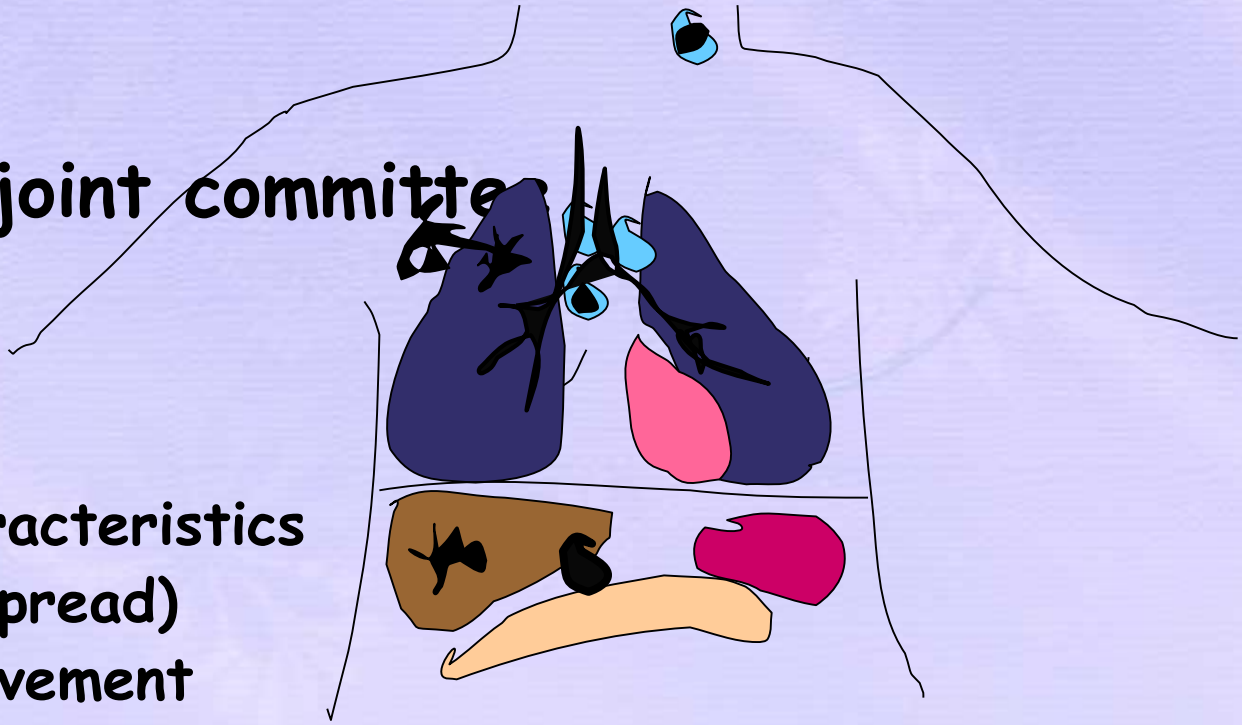
Paraneoplastic Syndromes

Remote effects not due to local effects of primary tumor or its metastases

- Fever
- Nephrotic syndrome
- Hypercalcemia
- Neurologic
- Skin manifestations
- Hypercoagulable State
- Endocrine syndrome…Malignant tumors may produce a number of peptide hormones whose secretion is not under normal regulatory control (ectopic hormone production).

Staging

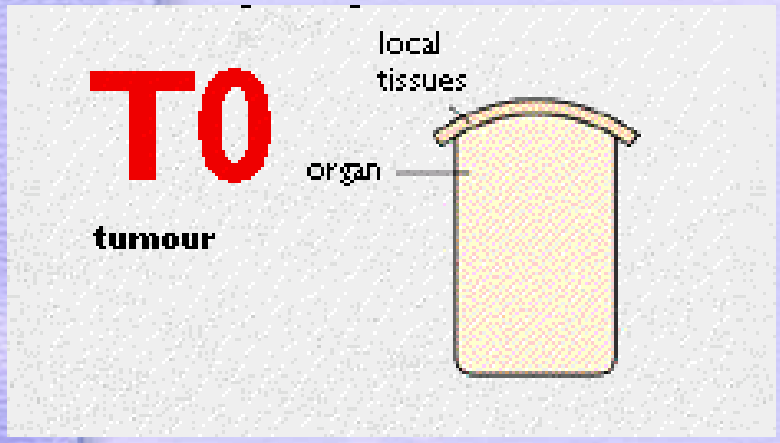
- Reflects degree of spread of a tumor, for an individual cancer patient
- Assigned at the time of diagnosis, may be updated as patient progresses
- 2 systems:
  *TNM,
  *American joint committe

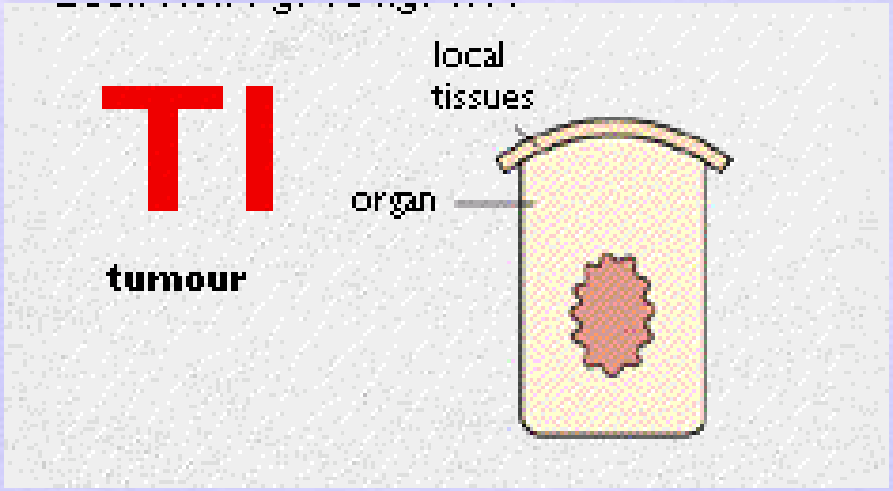


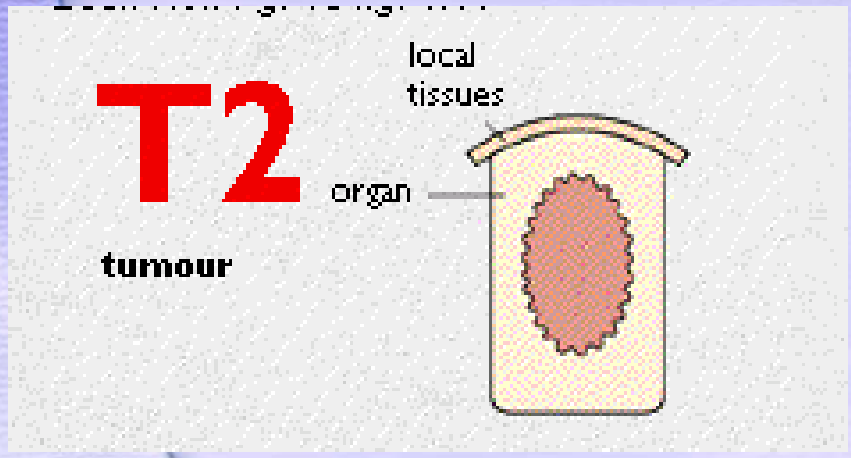
TNM

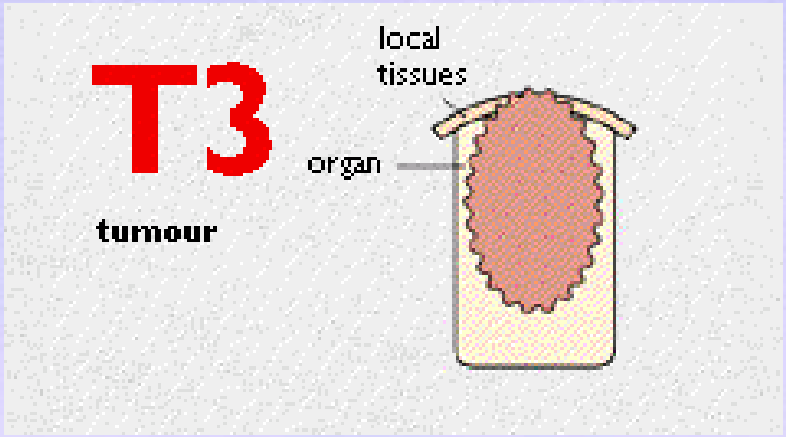
T Tumor characteristics (Size or local spread)
N Nodal involvement
M Metastasis

TNM Staging
T= primary tumor

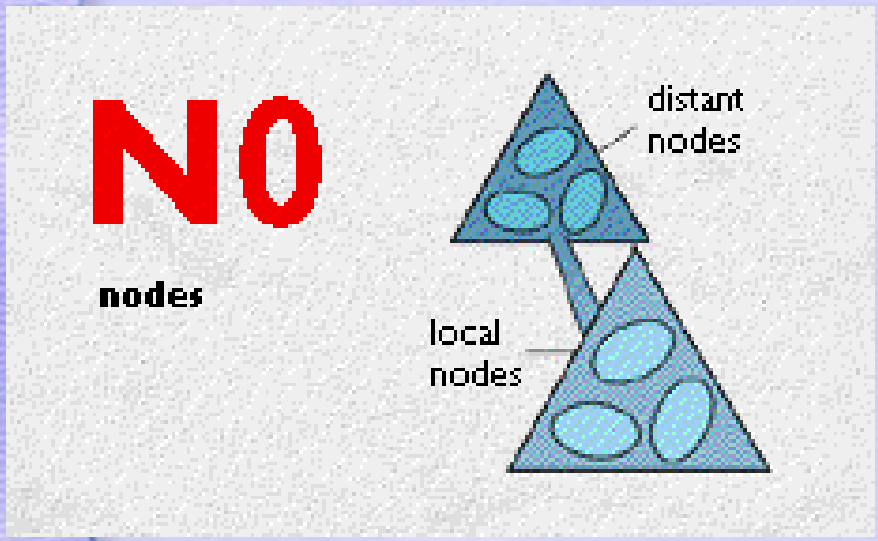


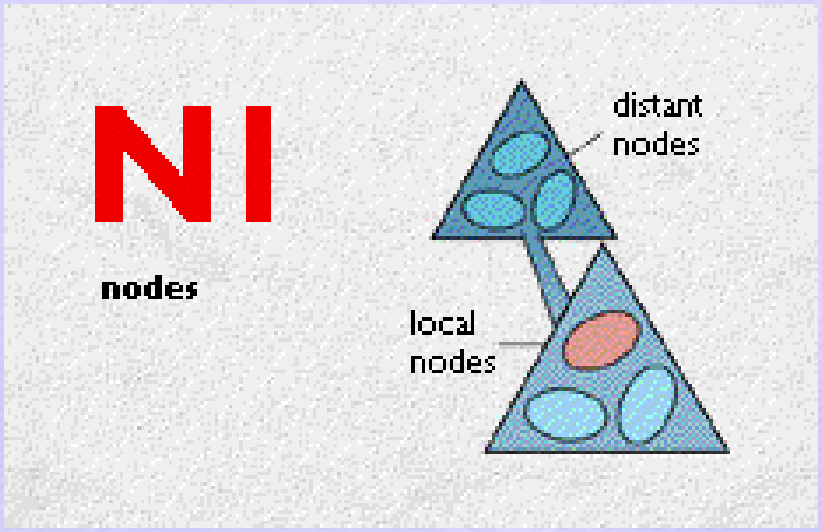


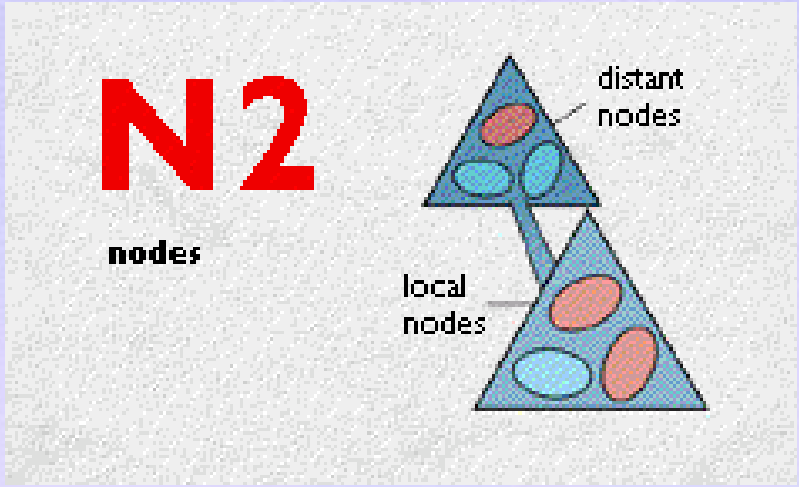




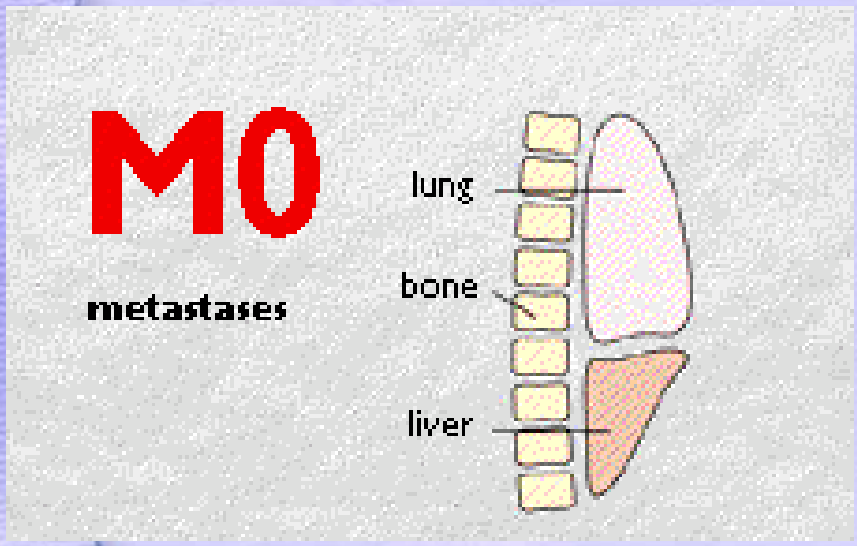
N= lymph node

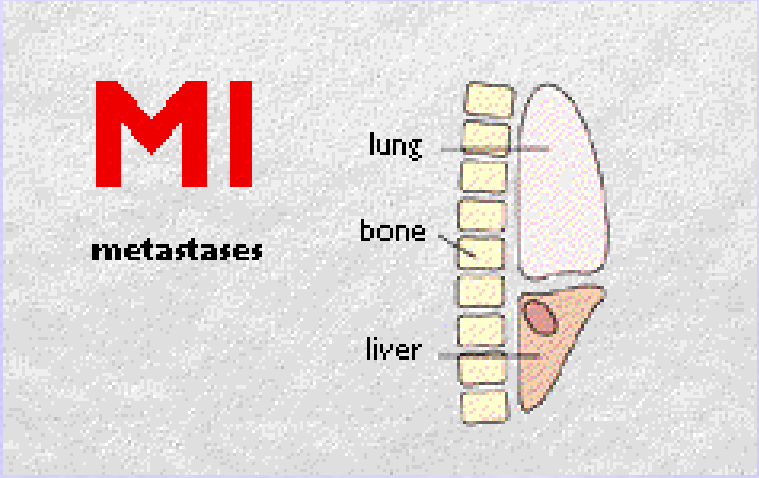

N0
nodes
distant
nodes
local
nodes

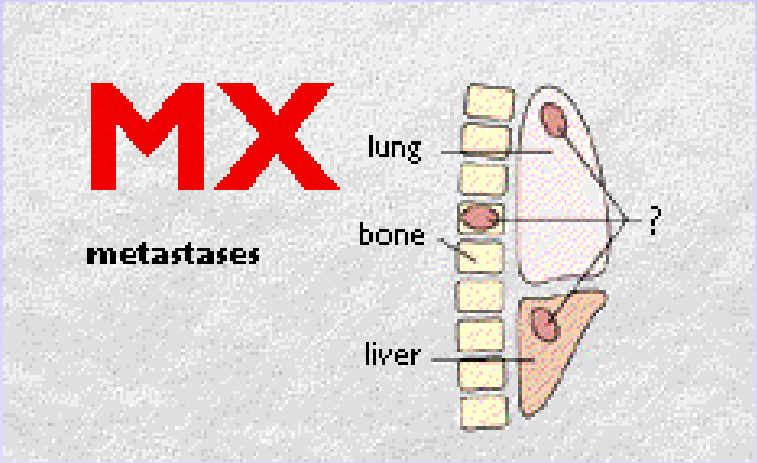

N1
nodes
distant
nodes
local
nodes


N2
nodes
distant
nodes
local
nodes

M= distant metastasis





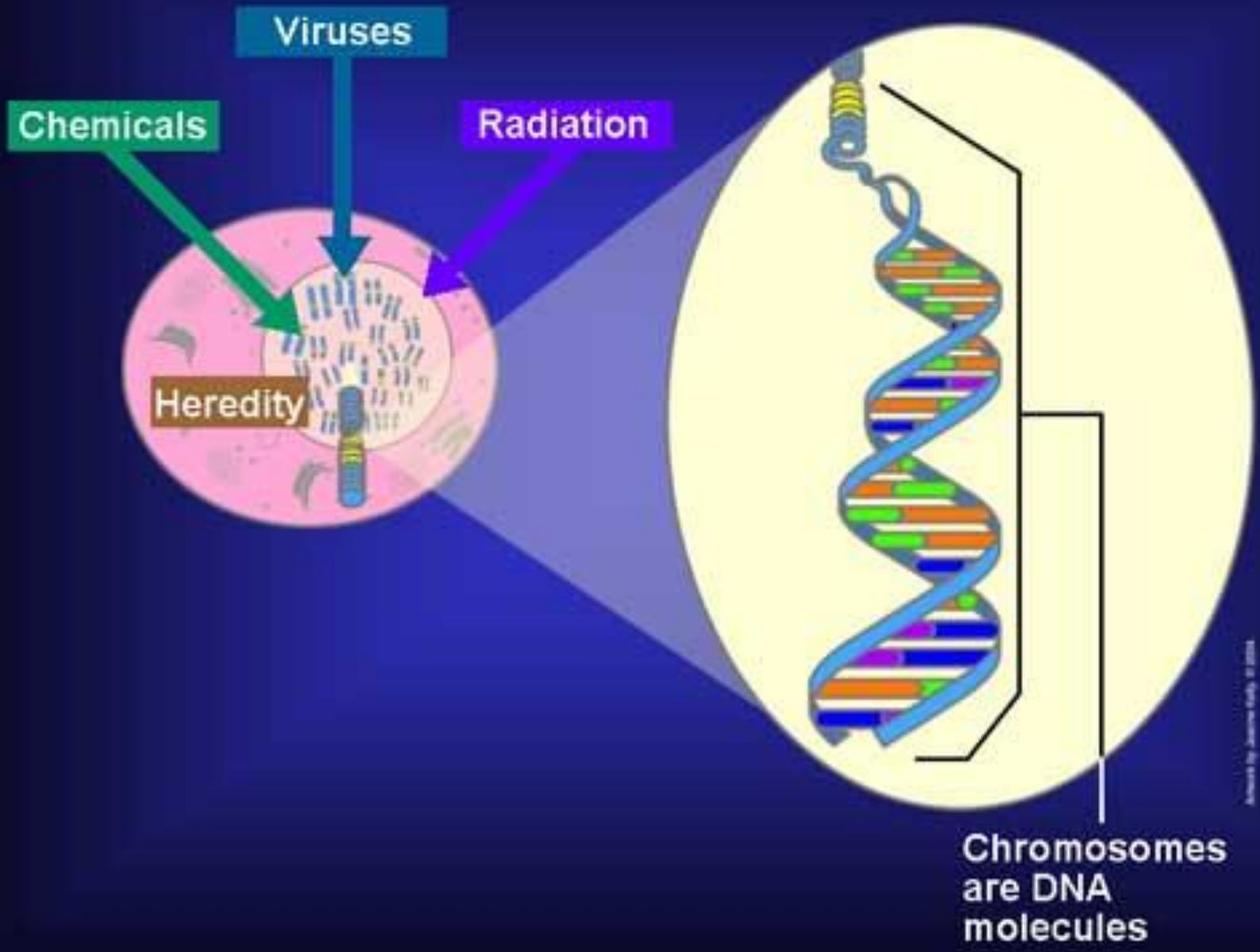


Carcinogenesis

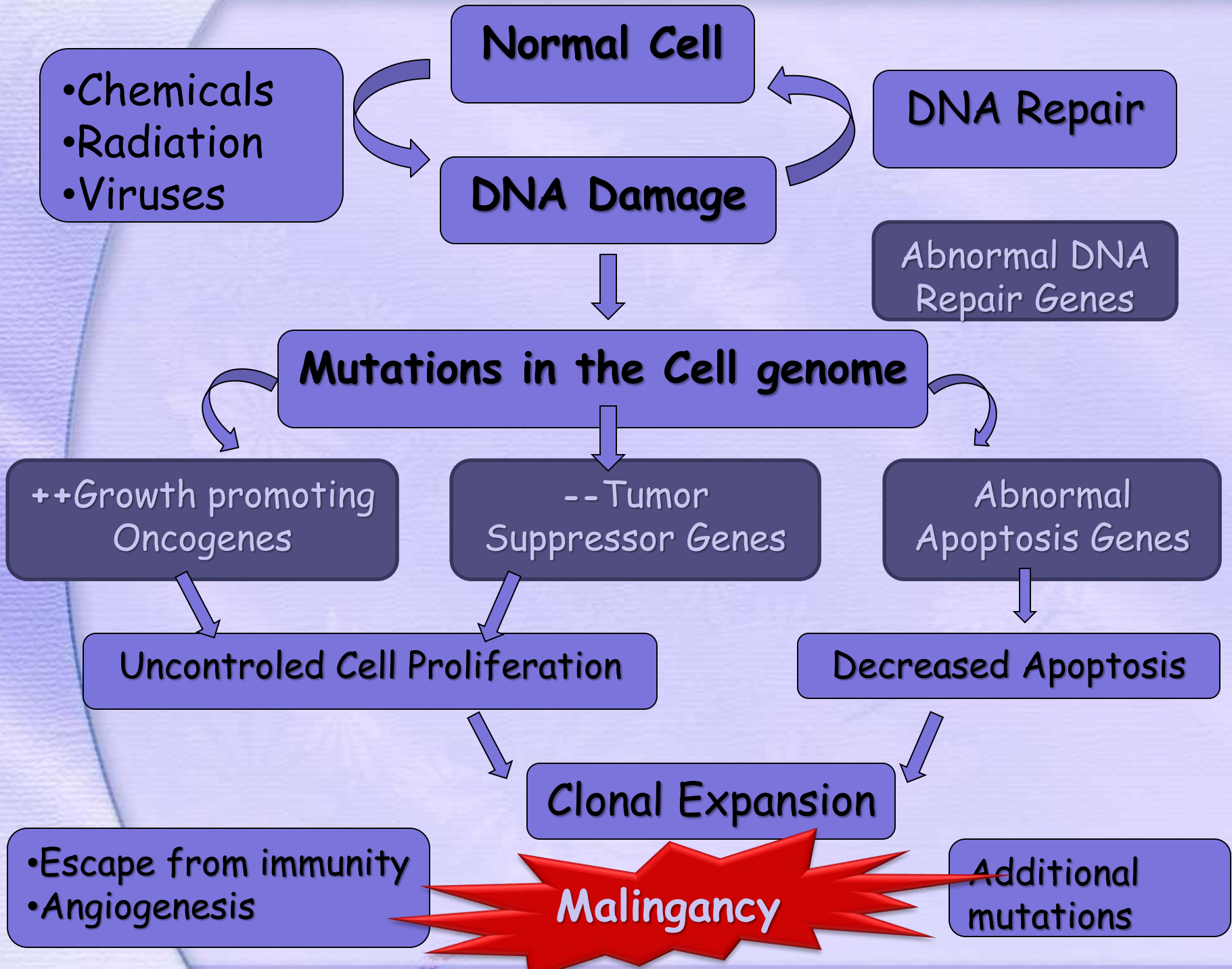
Q: WHO are the usual suspects?

1) Chemicals
2) Radiation
3) Infectious Pathogens

Genes and Cancer



NATIONAL CANCER INSTITUTE


Normal Cell
•Chemicals
•Radiation
•Viruses
DNA Repair
DNA Damage
Abnormal DNA Repair Genes
Mutations in the Cell genome
++Growth promoting Oncogenes
--Tumor Suppressor Genes
Abnormal Apoptosis Genes
Uncontroled Cell Proliferation
Decreased Apoptosis
Clonal Expansion
•Escape from immunity
•Angiogenesis
Malingancy
Additional mutations

1. Cancer is due to non-lethal genetic damage (Mutation) which may be acquired due to environmental factor as radiation, chemical or viruses or it may be inherited in the germ line.
2. The tumor mass is formed as a result of proliferation of this mutated cells.
3. The damage usually affects the genes which regulate cellular proliferation
4. Cancer is the result of a multi-step process.

Mutation of growth regulatory genes:

a) The growth promoting proto-oncogene: responsible for controlling normal growth and proliferation. Ex: EGFR

b) The growth inhibiting tumor suppressor genes: genes code the production of proteins that inhibit cell proliferation. Ex:P53 gene

c) Genes that regulate programmed cell death (Apoptosis): Antiapoptotic genes leads to prolongation of life span of cells. Ex: BCl2 gene

d) Genes involved in DNA repair: genes that control the expression ofDNA repairing enzymesEx; mismatch repair genes


Thank You